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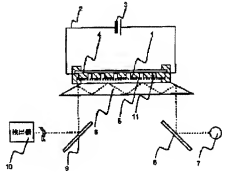
(54) **COOLING ELEMENT FOR BLOOD**

(57) Abstract:

PROBLEM TO BE SOLVED: To measure, with high sensitivity, the concentration of a biochemical component in whole blood by infrared spectroscopy by a method wherein a blood-cell filtration membrane is installed on the heat dissipating face side of a thermomodule and a meshlike or porous substrate is installed on the cooling face side of the thermomodule.

SOLUTION: Whole blood is dropped on a blood-cell filtration membrane 4. Blood cells in the whole blood which is dropped on the blood-cell filtration membrane 4 are left on the blood-cell filtration membrane 4, and blood plasma as a liquid is permeated through gaps 11 and a substrate 5 at a thermomodule 1 so as to reach an attenuation total-reflection prism 6. When the blood serum reaches the prism 6, a current flows from a DC power supply 3, heat on the cooling face side of the thermomodule 1 is absorbed, and the blood serum is cooled. On the other hand, the heat which is absorbed on the cooling face side is dissipated from the heat dissipating side of the thermomodule 1, the blood cells on the blood-cell filtration membrane 4 are not frozen even when the blood plasma on the cooling face side is frozen, and the concentration of a component is not changed due to hemolysis. When the whole blood is frozen and a solid component occupied in a liquid which remains due to freeze concentration amounts to about 80%, its freezing operation does not progress any more even at any low temperature.



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DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention]This invention relates to the blood cooling element used for the device and it which measure the biochemistry ingredient in blood by infrared spectroscopy by making into a sample whole blood (blood which has collected blood [containing a corpuscle]).
[0002]
[Description of the Prior Art]In recent years, in the clinical laboratory test field, in order to shorten the waiting time of the patient by inspection, shortening of analytical time is called for.
[0003]Conventionally, in the clinical laboratory test, in order to prevent change of the ingredient by hemolysis, the metabolic turnover of a corpuscle, etc., the plasma and the blood serum with which the corpuscle was removed from blood have been used as a sample. However, since time and time and effort are taken in centrifugal separation etc., removal of a corpuscle has been asked for the analytical skills in which whole blood measurement is possible.
[0004]Dry chemistry is described [in / which measure the biochemistry ingredient in blood by making the existing whole blood into a sample / the method and device / the 537th page] from a **** cough, the 7th volume, 1984, and the 534th page. Dry chemistry is analytical skills which trickle a sample into porous material on the film which carried out dry maintenance of the reaction reagent, advance a coloring chemical reaction in a film with the moisture in a sample, and quantify the concentration of an objective component. Although the dry chemistry of a test strip type and a multilayer analysis film mold is described here, in the dry chemistry corresponding to a whole blood sample, the corpuscle filtration membrane of the fiber for each to filter the corpuscle in whole blood independently as for the reagent layer holding a reagent is installed.
[0005]About the method which measures a biochemistry ingredient by infrared spectroscopy, it is applied, for example. The 95th page is described from the 85th page in

the 48th volume of spectroscopy (Applied Spectroscopy), No. 1, and 1994. Here, while measuring with the Fourier-transform-infrared-spectroscopy meter which used attenuated-total-reflection prism as the sample cell, six ingredients, such as quality of total protein in plasma and glucose, are measured with the non-reagent using a infrared spectrum. The high sensitivity-ized method of this technique is U.S. Pat. No. 5434411. It is set and indicated. It is the composition which this cools [composition] the liquid sample on attenuated-total-reflection prism from the upper part, makes the ingredient in a sample condense on prism by solidifying the moisture in a sample, and measures the infrared absorption spectrum of the surface of the sample which carried out ingredient concentration by attenuated-total-reflection prism.

[0006]

[Problem(s) to be Solved by the Invention]In order that the dry chemistry which is a biochemical analysis method which makes the conventional whole blood a sample might prepare many analysis elements according to a parameter, its running cost was high and it also had the problem of a dead stock. On the other hand, it is applied [said]. Although the biochemical analysis method using infrared spectroscopy which is described in the 95th page from the 85th page is low cost with a non-reagent, in the 48th volume of spectroscopy, No. 1, and 1994, Since sensitivity was bad, it was difficult to measure a low-concentration ingredient like uric acid and creatinine. U.S. Pat. No. 5434411 invented as a high sensitivity-ized method of infrared spectroscopy In the method currently set and indicated. When whole blood was made into a sample, in order to solidify a sample, the corpuscle hemolyzed, in order that constituent concentration might change or existence of a corpuscle might control coagulation, the enrichment factor fell and there was a problem that-izing could not be carried out [high sensitivity].

[0007]

[Means for Solving the Problem]An object of this invention is to measure biochemistry constituent concentration in whole blood to high sensitivity by infrared spectroscopy. In order to prevent decline in an enrichment factor by hemolysis and a corpuscle accompanying coagulation of a sample, a corpuscle filtration membrane was provided in the heat sinking plane side of a thermo module, and a substrate of reticulated or porous state was formed in the cooling surface side of a thermo module. A thermo module of a piece described by this invention carries out the series connection of the pi type element which made a pair a p-type semiconductor and an n-type semiconductor which are kinds of a thermoelement, for example, and connected by an electrode, and refers to what covered an electrode surface in both sides of an element with an insulator of one sheet, respectively.

[0008]

[Embodiment of the Invention]Drawing 1 is a sectional view of the composition of the primary detecting element of the hemanalysis device using the cooling element for blood which is the first example of this invention. The heat sinking plane of two or more thermo

modules 1 is arranged, it arranges on 1 flat surface seriate, the meantime is connected in series with the lead 2 which performed water proof and an insulation, and it connects with DC power supply 3. The corpuscle filtration membrane 4 furthermore formed in the heat sinking plane side of the thermo module 1 from the water permeability good fiber of glass fiber or cellulose is installed.

[0009]On the other hand, the porous or reticulated substrate 5 formed from the substance with copper high thermal conductivity is pasted up on the cooling surface of the thermo module 1 with the good adhesives of pyroductivity.

[0010]The whole blood which is a sample is dropped on the corpuscle filtration membrane 4. The corpuscle in the whole blood dropped on the corpuscle filtration membrane 4 remains on the corpuscle filtration membrane 4, and the plasma which is a fluid penetrates the gap 11 and the substrate 5 of the thermo module 1, and reaches on the attenuated-total-reflection (ATR) prism 6. For example, the gap 11 of a thermo module and the circumference of the substrate 5 are filled up with what formed construction material with sufficient water perviousness, such as cellulose, cellulose acetate, cellulose ester, polycarbonate, polytetrafluoroethylene, and glass fiber, in porous state, It is also possible to perform osmosis in the substrate 5 of plasma promptly according to capillarity.

[0011]If plasma reaches on the prism 6, current will flow from DC power supply 3, the endothermic of the heat by the side of the cooling surface of the thermo module 1 is carried out, and cooling of plasma is started. Even if the heat by which the endothermic was carried out radiates heat, it accumulates by the cooling surface side of an element from the allotropy child's 1 heat sinking plane side on the other hand and the plasma by the side of a cooling surface is frozen, the corpuscle on the corpuscle filtration membrane 4 is not frozen, and does not produce change of the constituent concentration by hemolysis, either. However, the heat sinking plane side of the element 1 prevents the superfluous rise of the temperature by heat dissipation, and in order to make regularity the cooling rate by the side of a cooling surface, while cooling at least, it needs to maintain it at constant temperature.

[0012]Whole blood is frozen, if the solid ingredient occupied in the fluid which remains by freeze concentration becomes just over or below 80%, however it may use low temperature, freezing will not progress any more, but it is reported that 20% of the water in a sample remains with a fluid. It is because this is left among solids, such as a corpuscle of a supersaturation state, while water has been a fluid, and icy crystal formation is obstructed. Therefore, by filtering a corpuscle component and freezing only plasma, an enrichment factor can be raised and high sensitivity-ization of infrared absorption can be attained.

[0013]After freezing of plasma is completed, the infrared absorption spectrum of the plasma constituent condensed by the surface of ATR prism 6 is measured. 0.6-25 micrometers emitted from the light source 7 It is reflected in the reflector 8 and infrared light enters into ATR prism 6. It is transparent, and insoluble to water and ATR prism 6 is formed in the infrared region from the crystal of a high refractive index, for example, zinc selenide,

germanium, silicon, sapphire, etc. Since the refractive index of the prism 6 is higher than the plasma and the atmosphere which touched the prism 6, the light which entered into the prism 6 causes total internal reflection by the interface. When carrying out total internal reflection, a part of lights [about 2-3 micrometers of] ooze out to the exterior of prism on infrared wavelength. Therefore, light oozes out also in the plasma which is a sample, and only the surface which the plasma constituent condensed can be measured. The light guide of the light which emitted the prism 6 is carried out in the detector 10 direction by the reflector 9.

[0014]Drawing 2 is a sectional view showing the composition of the thermo module used by this invention. It is what connected further in series pi type element which made the pair the p-type semiconductor 19 and the n-type semiconductor 20, and connected by the electrode 21 by the electrode, and has composition which sandwiched the electrode surface of the both sides of an element with the water proof insulator 22. The portion which the semiconductor of the end face of an element has exposed gives the water seal with polymers, such as silicon, in order to prevent degradation by the moisture of an element. The direction into which current flows can prescribe a cooling surface and a heat sinking plane.

[0015]Drawing 3 is the figure which looked at the shape of the thermo module used for the cooling element for blood which is the second example of this invention from the upper part. Although the composition of a cooling element laminates a substrate, a thermo module, and a corpuscle filtration membrane like drawing 1, it is not plurality but is composition which sandwiches the thermo module 23 of one sheet with a corpuscle filtration membrane and a substrate. The thermo module 23 connects pi type element in series in the shape of 99 box by an electrode, fills up the gap and the circumference between elements with polymers etc., and carries out a water proof insulation. The breakthrough 25 is formed in the polymer material of the gap of the wiring 24 of pi type element. This breakthrough 25 is passed and plasma reaches a substrate from a corpuscle filtration membrane.

[0016]Drawing 4 is a lineblock diagram of the primary detecting element of the hemanalysis device using the cooling element for blood which is the third example of this invention. In this example, the cooling element itself uses for the gap of the thermo module of drawing 1 or drawing 2 the composition which is not filled up with a porous material, and in order to shorten the time of plasma filtration, it establishes a pressurizing mechanism so that the heat sinking plane side of the thermo module 1 may be pressurized. This mechanism forces the box-like presser foot 14 connected to the pump 13 at the heat sinking plane side of the cooling element 12 for blood, sends air to the space which pressed down with the cooling element 12 and was made between 14 from the pump 13, and pressurizes the blood on the corpuscle filtration membrane 4 of the cooling element 12. The sealing compound 15 formed by silicone rubber etc. so that there might be no leak of air or a sample in the interface of the presser foot 14 and the cooling element 12 and the interface of the cooling element 12 and the jig of ATR prism 6 is arranged. By the supplied air from

the pump 13, the blood on the corpuscle filtration membrane 4 is pressurized, and only plasma penetrates the corpuscle filtration membrane 4 and reaches on ATR prism 6 from the substrate 5.

[0017]Drawing 5 is a basic constitution figure of the optical system of the hemanalysis device which used the cooling element for blood of this invention. The infrared light emitted from the light source 7 spreads ATR prism 6, and enters into the interferometer 16. Infrared light enters into the detector 10, after producing phase contrast with the interferometer 16. The signal detected by the detector 10 is inputted into the computer 18 through A/D converter 17. In the computer 18, the Fourier transform of the signal is carried out and the absorbance of each wavelength is computed.

[0018]For example, when measuring the creatinine concentration in blood with the hemanalysis device of this invention, the infrared absorption spectrum of the blood which is a sample is measured using this invention, the absorbance to 1700-1300cm^{-1} is substituted for a measuring formula, and concentration is computed. A measuring formula is partial beforehand. Leased It computes by the measuring method using multivariate analyses, such as the square (Partial Least Squares:PLS) method, etc., and the recorder in the computer 18 is made to memorize.

[0019]Drawing 6 is an infrared absorption spectrum of the blood showing the effect of this invention. As for the spectrum a, the spectrum and the spectrum b which were measured at the usual room temperature are U.S. Pat. No. 5434411. The spectrum measured by the method currently indicated and the spectrum c are spectra measured by this invention. In the spectrum b, in order that a corpuscle might block concentration, it was by high sensitivity-ization of an about [room temperature ratio 4 time], but since the spectrum c by this invention removed the corpuscle, it attained high sensitivity-ization of an about [room temperature ratio 20 time].

[0020]

[Effect of the Invention]According to this invention, the biochemistry constituent concentration in blood can be measured to high sensitivity by making whole blood into a sample.

[Translation done.]

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CLAIMS

[Claim(s)]
[Claim 1]A cooling element for blood consisting of a corpuscle filtration membrane installed in a heat sinking plane of a substrate of porosity or mesh shape, two or more thermo modules which opened and allotted an interval in two dimensions [cooling surface] in contact with this board, and this thermo module.
[Claim 2]It molds in tabular by using as 99 boxes what carried out two or more series connections of the pi type thermoelement which made a pair a p-type semiconductor and an n-type semiconductor, and was joined, A thermo module which covered a water proof insulating material and provided two or more breakthroughs in a water proof insulating material between elements so that it might be filled up with between elements and the whole element might be covered, A cooling element for blood consisting of a corpuscle filtration membrane installed in a substrate of porosity allotted so that a cooling surface of this module might be touched, or mesh shape, and a heat sinking plane of this module.
[Claim 3]The cooling element for blood according to claim 1 using a thermo module which carried out the water proof insulation of the circumference.
[Claim 4]The cooling element for blood according to claim 1 or 2, wherein porosity or a mesh shape board, a thermo module, and a corpuscle filtration membrane which were made to laminate cover the end face of three layers with a frame and are fixed.
[Claim 5]The cooling element for blood according to claim 1 filling up a gap of a thermo module with porous material so that a substrate and a corpuscle filtration membrane may be touched.
[Claim 6]The cooling element for blood according to claim 2 by which being filled up with porous material so that a substrate and a corpuscle filtration membrane may be touched into a breakthrough formed in a thermo module.
[Claim 7]A cooling element for blood, wherein the corpuscle filtration membrane according to claim 1 or 2 consists of what formed textiles, such as glass fiber and a cellulose cloth, in the shape of a film.
[Claim 8]The cooling element for blood according to claim 1 or 2 which is reticulated or is

characterized by a substrate of porous state being more than $\sim^{1}s\sim^{1}K\sim^{1}$ 0.8 cal cm, and being [substrate] insoluble to water in thermal conductivity.

[Claim 9]A cooling element for blood, wherein the porous material according to claim 5, 4, or 6 consists of construction material with sufficient water perviousness, such as cellulose, cellulose acetate, cellulose ester, polycarbonate, polytetrafluoroethylene, and glass fiber.

[Claim 10]It is a hemanalysis device which has a detector which detects light which emitted light from an infrared light source, a spectral means, and this light source from attenuated-total-reflection prism which carries out ON outgoing radiation, and this attenuated-total-reflection prism, and a computer which processes a detected signal, A hemanalysis device installing the cooling surface side of the cooling element for blood according to claim 1 or 2 on attenuated-total-reflection prism via a substrate and a sample.

[Claim 11]The infrared light source according to claim 10 is 0.6-25 micrometers. A hemanalysis device irradiating with light of wavelength.

[Claim 12]The hemanalysis device according to claim 10 making the Fourier spectrum into a spectral means.

[Claim 13]A hemanalysis device the attenuated-total-reflection prism according to claim 10 is transparent in light with which the infrared light source of zinc selenide, germanium, silicon, sapphire, etc. according to claim 11 irradiates, and becoming water from an insoluble substance.

[Claim 14]A hemanalysis device, wherein atmospheric pressure by the side of a heat sinking plane of the cooling element for blood according to claim 10 is higher than atmospheric pressure by the side of a cooling surface.

[Translation done.]